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Alimentary Tract

The natural history of achalasia: Evidence of a continuum—"The evolutive pattern theory"☆

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ABSTRACT

Background: It is currently unclear if the three manometric patterns of esophageal achalasia represent distinct entities or part of a disease continuum. The study's aims were: a) to test the hypothesis that the three patterns represent different stages in the evolution of achalasia; b) to investigate whether manometric patterns change after Laparoscopic-Heller-Dor (LHD).

Methods: We assessed the patients diagnosed with achalasia who underwent LHD as their first treatment from 1992 to 2016. Their symptoms were scored using a detailed questionnaire for dysphagia, food-regurgitation, and chest pain. Barium-swallow, endoscopy, and esophageal-manometry were performed before and 6 months after surgery.

Results: The study population consisted of 511 patients (M:F = 283:228). Patients' demographic and clinical data showed that those with pattern III had a shorter history of symptoms, a higher incidence of chest pain, and a less dilated gullet ($p < 0.001$). All patients with a sigmoid-shaped mega-esophagus had pattern I achalasia. One patient with a diagnosis of pattern III achalasia developed pattern II at a follow-up manometry before surgery.

At a median follow-up of 30 months (IQR 12–56), the outcome of surgery was positive in 479 patients (91.7%).

All patients with pattern I preoperatively had the same pattern after LHD, whereas more than 50% of patients with pattern III before treatment showed pattern I or II after surgery.

Conclusions: This study supports the hypothesis/theory that the different manometric patterns represent different stages in the evolution of the disease—where pattern III is the earliest stage, pattern II an intermediate stage, and pattern I the final stage.

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1. Background

Esophageal achalasia is a motility disorder characterized by the lack of esophageal peristalsis and failure of the lower esophageal sphincter (LES) to relax. Achalasia is a rare disease with an estimated incidence between 0.3 and 1.6 per 100,000 population a year [1,2]. Symptoms include slowly worsening dysphagia (for solids and liquids), food regurgitation, and chest pain [3,4].

Achalasia is a disease that develops slowly, which is why patients often present late in the course of this disease, when their clinical situation, symptoms, and anatomical and physiological abnormalities have become severe.

According to the Chicago Classification (CC) associated to high-resolution manometry studies, esophageal achalasia is now distinguished on the basis of three clinically relevant patterns emerging at esophageal manometry: pattern I, achalasia with minimal esophageal pressurization; pattern II, achalasia with pan-esophageal compression; and pattern III, achalasia with spasm [5–7]. It is currently not clear, however whether these three manometric phenotypes represent three different diseases, or different stages of the same disease, with the possibility of a transition or progression from one to another. We recently published a prospective preliminary study on achalasia patients assessed with

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high-resolution manometry (HRM), in which our group first raised the hypothesis that the three patterns might represent three different stages of the same disease [8].

The aims of the present study were: a) to test the hypothesis that the three manometric patterns represent different stages in the evolution of esophageal achalasia in a large group of achalasia patients; and b) to investigate whether these manometric patterns change after laparoscopic Heller-Dor myotomy (LHD).

2. Material and methods

We assessed patients diagnosed with esophageal achalasia who underwent LHD as their first treatment from 1992 to May 2016 at the Department of Surgical, Oncological, and Gastroenterological Sciences, University of Padova (Italy). Patients who had already been treated with botulinum toxin injections, pneumatic dilations, per-oral endoscopic myotomy (POEM), or surgical myotomy were excluded from the study. Esophageal achalasia was diagnosed on the basis of accepted esophageal motility characteristics (i.e. no peristalsis in the esophageal body and impaired LES relaxation on swallowing) together with clinical and radiological/endoscopic signs [1,4]. Patients' demographic and clinical data were collected using a dedicated questionnaire. The scores for dysphagia, food regurgitation and chest pain were calculated by combining the severity of each symptom (0–6) with its frequency (0 = never, 1 = occasionally, 2 = once a month, 3 = every week, 4 = twice a week, 5 = daily). The symptom score was the sum of the dysphagia and food regurgitation scores, while the chest pain score was considered separately [9].

Before LHD, all patients had barium swallow X-rays to assess the diameter and shape of the esophagus, and traditional or high-resolution esophageal manometry and endoscopy to rule out cardia malignancies.

The surgical technique for LHD has been described in detail elsewhere [10], and was performed in the same fashion by 6 staff surgeons. The postoperative follow-up included examining patients 1, 6 and 12 months after their operation, and every 2 years thereafter, using the same questionnaire as was administered preoperatively. Barium swallow was required 1 month after LHD and in the event of recurrent dysphagia or food regurgitation. Esophageal manometry, using the same technique as before surgery, was performed 6 months after LHD, together with 24-h pH monitoring to check for any abnormal acid exposure of the distal esophagus. Endoscopy was recommended 12 months after surgery, and then every 2 years thereafter, to identify and control any complications of GERD and rule out any neoplastic degeneration. Treatment failure was defined as a postoperative symptom score higher than the 10th percentile of the preoperative score for the group of patients as a whole (i.e. >8) [7,11].

This was an observational study and all the procedures were routinely performed for the diagnosis and follow-up of patients with esophageal achalasia undergoing LHD, so institutional review board approval was not required. The study was approved by the Research-Ethical Committee (RS-SM 2016) of our Department of Surgical, Oncological, and Gastroenterological Sciences (University of Padova).

2.1. Evolution in manometric pattern

Patients all underwent conventional manometry (CM) or high-resolution manometry (HRM). A pneumohydraulic perfusion system was used for CM (Menfis, Bologna, Italy) and the procedure has been described in detail elsewhere [7]. All conventional manometric tracings obtained before 2010, were reviewed and reclassified according to their manometric pattern, whereas the HRM data were collected prospectively from 2010 onwards. The manometric patterns identified on CM were originally classified as proposed by our group in a previous study: pattern I achalasia when 8/10 swallows elicited contractions with an amplitude <30 mmHg; pattern II when 2 or more contractions had an amplitude >30 mmHg; and pattern III when at least two spastic waves were detected (lasting >6.0 s with an amplitude >70 mmHg) [7]. HRM was performed with a catheter 4.2 mm in diameter with 36 solid-state circumferential sensors spaced at 1 cm intervals and spanning the whole esophagus (Medtronic, Covidian. USA). The Chicago classification was used for the HRM findings, defining achalasia as: pattern I when there was no distal esophageal pressurization to >30 mmHg in >8/10 swallows (Fig. 1a); pattern II when at least 2 test swallows were associated with a panesophageal pressurization >30 mmHg (Fig. 1b); and pattern III when patients had at least 20% of premature contractions (Distal latency <4.5 s) [6] (Fig. 1c).

2.2. Statistical analysis

Continuous data were expressed as medians and interquartile ranges, categorical data as numbers and percentages. Continuous and categorical data were compared between the three groups of patients with pattern I, II and III achalasia using the Kruskal–Wallis test and Fisher's test, respectively. Variations between pre- and postoperative findings were assessed using Wilcoxon's test. The association between failure of LHD treatment and patients' demographic and clinical characteristic was assessed using the Mann-Whitney test and Fisher's test. A p-value of less than 0.05 was considered significant.

3. Results

3.1. General outcome of surgery

During the study period, 511 patients (283 men and 228 women; median age 46 years, IQR 33–56) underwent LHD, and formed the study population. The LHD procedure was completed laparoscopically in all but two cases. One patient died on postoperative day 1 due to an acute myocardial infarction. Esophageal mucosal perforations occurred during the procedure in 15 patients, and were repaired intraoperatively in all cases. Two lesions were identified on water-soluble contrast swallows on the first postoperative day.

Overall, with a median follow-up of 36 months (IQR 15–60), the outcome after LHD was still favorable in 479 patients (91.7%), while 42 patients had recurrent achalasia symptoms. The two predictors of final outcome were the preoperative manometric pattern and the chest pain score ($p < 0.001$, Table 1). Vis-à-vis the preoperative manometric achalasia pattern, the incidence of failure was: 10.4% in pattern I, 4.6% in pattern II and 25.6% in pattern III. All patients with recurrent symptoms were treated with one or more complementary endoscopic pneumatic dilations using Rigiflex balloons (30, 35 or 40 mm), which cured their residual symptoms in all cases. At postoperative 24-h pH-monitoring, 9.8% of the patients (34 of 346 who agreed to take the test) revealed a pathological acid exposure of the distal esophagus.

3.2. Manometric pattern

After assessing and reviewing their preoperative manometric picture, 231 patients (45.2%) were classified as having pattern I, 241 (47.2%) had pattern II, and 39 (7.6%) had pattern III. One patient diagnosed with pattern III achalasia had refused any treatment and revealed pattern II at a follow-up manometry performed 36 months later due to gradually worsening dysphagia. The patient underwent successful LHD.

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